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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,517	02/02/2001	Gregory Grabowski		1629

26874 7590 10/30/2003
FROST BROWN TODD, LLC
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EXAMINER

WEBER, JON P

ART UNIT PAPER NUMBER

1651

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<p style="text-align: center;">Office Action Summary</p>	Application No. 09/775,517	Applicant(s) GRABOWSKI ET AL.	
	Examiner Jon P Weber, Ph.D.	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 10-68 is/are pending in the application.
- 4a) Of the above claim(s) 37-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 10-35 and 66-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>9/9/03</u> | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
6) <input type="checkbox"/> Other: _____ |
|---|---|

Status of the Claims

The response with amendments filed 09 September 2003 has been received and entered. Claims 1-4 and 10-68 have been presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

This application contains claims 37-65 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection **must** include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-4, 10-35 and 66-68 remain to be considered on the merits.

Claim Rejections - 35 USC § 103

Claims 1-36 and 66-68 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (1986), Bond et al. (1991), Pomerantz et al. (1993), Waters et al. (1994) and Escary et al. (1998) in view of Coates et al. (1986).

It is argued that Chan et al. (1986), Bond et al. (1991), Pomerantz et al. (1993), Waters et al. (1994) and Escary et al. (1998) each individually only increase LAL indirectly by secondary induction and do not teach direct administration of LAL to reduce atherosclerotic plaques. It is also argued that Escary et al. (1999) provided a surprising finding that overexpression of HSL

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lead to increased susceptibility to atherosclerosis. Hence, Escary et al. (1999) teaches away from using HSL to induce LAL as a means of reducing atherosclerosis.

The interpretation of Escary et al. (1999) offered in the response is not exactly what they said. The conclusion was that simply increasing cholesteryl-ester hydrolysis without concomitantly decreasing ACAT activity or increasing cholesterol efflux, is not sufficient to protect against atherosclerosis. Thus, rather than teach away from the instantly claimed invention, Escary et al. (1999) offers that the situation is more complicated than simply increasing the LAL activity. The reason being that the free cholesterol produced is efficiently reesterified by ACAT. Further study was suggested to determine if the increased susceptibility to atherosclerosis was due to overexpression of HSL or the result of secondary effects on cholesterol trafficking, inflammatory response and expression of cytokines and receptors.

This brings us back to the original rejection of therapeutic treatment of an enzyme deficiency. To reiterate, there are only three possible ways of remedying an enzyme deficiency: 1) adding the enzyme exogenously, 2) inducing an increase in endogenous production by means of secondary agents, or 3) using gene therapy to introduce and express the desired enzyme. It was pointed out in the Office action of 01 April 2003 that gene therapy has not been very successful. The art relied upon establishes the use of secondary inducing agents to increase LAL for such treatment. It was argued that it is well known in the art to remedy an enzyme deficiency by exogenous addition of enzyme. For example, thrombotic events are often treated by addition of clot dissolving enzymes such as streptokinase, protein C and TPA. Such events may also be treated by compounds which activate the natural clot dissolving pathways. Hence, it is known in

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the art to use both direct addition of an enzyme or compounds that induce the enzyme for treating an enzyme deficiency or increasing an enzyme activity.

Hence, a person of ordinary skill in the art would be reasonably apprised of the alternative methods of increasing an enzyme activity to treat a disease state. Since, the induction method is well established by the relied upon art, and the gene therapy method is still "pie-in-the-sky", the only other possible alternative is direct administration of the enzyme which is what is instantly claimed.

Applicant's arguments filed 09 September 2003 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 103 is adhered to for the reasons of record and the additional reasons above.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

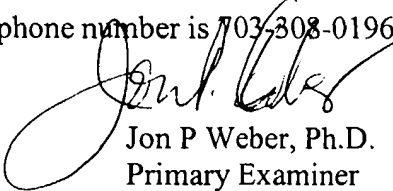
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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
29 October 2003